

AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph starting on page 2, line 7 of the specification with the following paragraph:

A microarray is an array of positionally-addressable binding (e.g., through hybridization) sites on a support. Each of such binding sites comprises a plurality of biopolymer molecules of a probe bound to the a predetermined region on the support. Microarrays can be fabricated in a number of ways, including immobilization of pre-synthesized probes on the support or the in situ synthesis of probes on the support. For example, immobilization of pre-synthesized probes can be done robotically as described in DeRisi et al. (1997, *Science* 278(5338):680-6) or by inkjet. In situ synthesis can be accomplished by different means, including using inkjet technology or by light-activated synthesis (Holmes et al., 1995, *Biopolymers* 37(3): 199-211; Jacobs et al., 1994, *Trends Biotechnol.* 12(1): 19-26; and Fodor et al., 1991, *Science* 251 (4995):767-73). In either case of in situ synthesis, chemical reactions take place on the support in which a monomer or monomers are added to the biopolymer. As the biopolymer chain grows, however, there is a chance that one or more of the synthesis cycles may fail (either fully or partially) thereby producing a probe that lacks one or more of the intended monomers. Synthesis efficiency depends on multiple factors including reagent purity, reaction time, correct alignment of the inkjet head, etc. Defects in any of these processes can result in inefficient addition of a monomer or monomers to the growing biopolymer chain.

Please replace the paragraph starting on page 2, line 24 of the specification with the following paragraph:

In addition, in the case of an inkjet-synthesized microarray, a synthesis defect may also occur when one of the nozzles of the inkjet head fails to deliver a reagent properly (e.g., if the nozzle becomes temporarily or permanently obstructed). A nozzle failure refers to any malfunction of an individual ink jet nozzle. If a nozzle fails to deliver the desired solution required for biopolymer addition, it is sometimes referred to as being “clogged.” A nozzle failure can occur at any point during microarray synthesis. A failure at the beginning of the synthesis may be due to insufficient priming of new reagents through the nozzles. A nozzle failure can also occur after the printing of a set of microarrays has begun if, e.g., there are trapped air bubbles or particulates. Nozzle failures can be detected and corrected before a microarray is synthesized. Before the start of each synthesis batch and at the end of each

synthesis batch every nozzle on the printhead can be tested to make sure that it is properly functioning. This can be done by placing a clean substrate on top of the head assembly before forcing each nozzle to extrude a small amount of liquid. If all nozzles are working properly, there will be a drop of liquid corresponding to each nozzle. If, however, one or more nozzles ~~is are~~ malfunctioning, the ~~drop drops~~ corresponding to ~~that those~~ nozzle ~~position is positions~~ ~~will be~~ missing. Because of the small size of the drops, a nozzle failure can be overlooked occasionally due to human error, and an array will be synthesized that shows evidence of a nozzle failure. Currently there exists a need for a more reliable method to determine if synthesis failures have occurred and, if so, where and when they happened during the course of microarray synthesis. Whereas it is possible to perform quality control on pre-synthesized probes by conventional DNA sequencing, by mass spectroscopy, or by other means, methods to assess the quality of probes synthesized in situ are lacking.

Please replace the paragraph starting on page 3, line 12 of the specification with the following paragraph:

This application describes a method designed to assess the quality of microarray synthesis. The herein disclosed invention describes methods for the design and production of quality control probes on ~~the microarray~~ microarrays and methods for analysis of the information obtained from microarray processing that permit the determination of the overall quality of synthesis as well as the identity of the synthesis cycle most likely to have been defective. This invention also includes a database that contains information concerning the position and identity of the quality control probes on ~~the microarray~~ microarrays.